Meeting of the Board of Scientific Counselors, Office of Infectious Diseases
Centers for Disease Control and Prevention
Tom Harkin Global Communications Center
Atlanta, Georgia

December 10, 2014

A 1-day, open public meeting of the Board of Scientific Counselors (BSC), Office of Infectious Diseases (OID), was held on December 10, 2014, at the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia. In addition to Board members and CDC staff, the meeting was attended by representatives of several public health partner organizations (appendix).

The meeting included updates from OID, followed by an update and discussion about CDC efforts to enhance laboratory safety. Reports were also provided by the BSC Antimicrobial Resistance Working Group (ARWG), the Infectious Disease Laboratory Working Group (IDLWG), and the Food Safety Modernization Act (FSMA) Surveillance Working Group (FSMA SWG), which presented its FY 2014 annual report for BSC approval. The meeting also included updates on the ongoing outbreaks caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV), enterovirus D68 (EV-D68), and Ebola virus. The update on CDC's response to the Ebola outbreak was followed by a discussion about issues related to long-term outbreak response efforts.

➢ OPENING REMARKS

BSC Chair Dr. Ruth Berkelman, Rollins Professor, Emory University, called the meeting to order and was joined in welcoming participants and facilitating introductions by Dr. Rima Khabbaz, CDC Deputy Director for Infectious Diseases, and Robin Moseley, the BSC/OID Designated Federal Officer. Dr. Berkelman welcomed four new Board members: Michael Brady, Associate Medical Director, Nationwide Children's Hospital, Columbus, Ohio; Tim Jones, State Epidemiologist, Tennessee Department of Health; Ruth Lynfield, Epidemiologist and Medical Director, Infectious Disease Division, Minnesota Department of Health; and Lee Riley, Professor of Epidemiology and Infectious Diseases and Chair, Division of Infectious Diseases and Vaccinology, University of California, Berkeley School of Public Health (Dr. Riley was unable to attend). Dr. Berkelman also welcomed two new liaison representatives: Elizabeth Marlowe, Assistant Director of Microbiology-Molecular Testing, Southern California Permanente Medical Group; and Guillermo Ruiz-Palacios, Professor and Director, National Institutes of Health and Tertiary Referral Hospitals, Mexico Ministry of Health.

➢ OID UPDATES

Dr. Khabbaz provided updates on current OID activities and their roles in advancing CDC's strategic priorities: improve health security at home and around the world; better prevent the leading causes of illness, injury, disability, and death; and strengthen public health/healthcare collaboration. Topics covered in her updated included

- The FY 2015 Emergency Request to Congress for $1.83 billion to fight Ebola
- Outbreaks of EV-D68 and MERS-CoV (described in detail later in the meeting, see pages 17-20)
- Intensified efforts to improve human papillomavirus (HPV) vaccine coverage. Approval of a 9-valent vaccine appears to be near, and the HPV vaccine schedules may be reduced from three doses to two.
- HIV prevention campaigns, including *Act Against AIDS*. A *Federal Register* notice about draft recommendations for providers counseling patients and parents regarding male circumcision and

preventing HIV infection and sexually transmitted infections (STIs) will be posted on Friday, December 12.

- Publication of the *National Strategy for Combating Antibiotic-Resistant Bacteria* (CARB), along with a report from the President's Council of Advisors on Science and Technology (PCAST) entitled *Combating Antibiotic Resistance,* and the launch of a $20 million prize sponsored by the National Institutes of Health (NIH) and the Biomedical Advanced Research and Development Authority (BARDA) to facilitate development of a rapid diagnostic test to identify resistant bacterial infections at the point of patient care. Proposed increases in the FY 2015 President's Budget to address antimicrobial resistance (AR) issues include $30 million to support CDC's *Detect and Protect Initiative* and $14 million for the National Health Safety Network.
- Progress in achieving polio eradication. Only 6 wild polio virus cases had been reported in Nigeria as of December 3, 2014, suggesting that Nigeria may soon be polio-free.
- October marked the 20th anniversary of the Vaccines for Children Program (VFC). VFC has been credited for preventing an estimated 322 million illnesses and saving ~732,000 lives.
- CDC held its first annual "AMD Day" in September, with 4 presentations and 22 posters
- During 2014, *Vital Signs* articles were published on antibiotic use in hospitals, outbreaks of norovirus, and efforts to ensure that HIV patients receive treatment and stay in care.
- The International Conference on Emerging Infectious Diseases (ICEID) has been rescheduled to August 24-25, 2015.

Dr. Khabbaz also announced the following awards and staff changes:

Awards

- Rana Hajjeh, Director of the Division of Bacterial Diseases, National Center for Immunization and Respiratory Diseases (NCIRD), received the 2014 "Federal Employee of the Year" award for her work leading the GAVI Hib Initiative
- Denise Cardo, Director of the Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), received the 2013 HHS Secretary's Award for Meritorious Service, honoring her achievements toward the elimination of healthcare-associated infections (HAIs)
- Alexander (Sasha) Klimov, former Chief of the Virus Surveillance and Diagnosis Branch in NCIRD's Influenza Division, was posthumously awarded the Sigma Xi 2014 Walter R. Dowdle Award
- Mark Pallansch, Director of NCIRD's Division of Viral Diseases, and the Polio Eradicators team, received the Franz Edelman Award for Achievement in Operations Research and the Management Sciences
- The *Listeria* Whole-Genome Sequencing (WGS) Surveillance Project, a collaboration among CDC, the U.S. Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the Association of Public Health Laboratories (APHL), received the HHS (U.S. Department of Health and Human Services) Innovates Award; the CDC *Using Motion Comics to Educate Young People About HIV and STDs* project received an HHS Innovates honorable mention

Staff Changes

- CDC is actively recruiting for the new position of Associate Director for Laboratory Science and Safety (see page 3)
- New appointments include
  - Nancy Messonnier, Deputy Director of NCIRD
  - Eugene McCray, Director, Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (NCHHSTP)
  - Phil Lobue, Director, Division of Tuberculosis Elimination, NCHHSTP

- Inger Damon, Director, Division of High-Consequence Pathogens and Pathology, NCEZID. Dr. Damon is also Incident Manager of CDC's Ebola response.

- Departures include
  - Nancy Cox, Director of NCIRD's Influenza Division, who retired from CDC after 37 years of service
  - Stephen Morse, Associate Director for Environmental Microbiology, NCEZID, who retired after more than 30 years of service
  - Larry Pickering, Senior Advisor to the NCIRD Director and Executive Secretary of the Advisory Committee on Immunization Practices (ACIP) will retire from CDC in March 2015
  - Kris Sheedy, NCIRD's Associate Director of Communication Science, is leaving CDC in January 2015

➢ **CDC Lab Safety Efforts—Update and Discussion**

Leslie Dauphin, interim lead for laboratory safety activities at CDC, reviewed the activities of CDC's internal Laboratory Safety Improvement Workgroup (LSIW). This group was established in July 2014 as part of CDC's response to recent laboratory safety incidents. The LSIW was charged with

- Reviewing requests to resume transfers of biological materials from BSL-3 and -4 laboratories following a moratorium. Thus far, 51 out of 53 CDC laboratories have resumed full operations.
- Overseeing an agency-wide inventory of biological materials. The inventory is being conducted in two steps: a rapid "Clean Sweep" completed in September to identify select agents and toxins, including those at CDC's long-term storage facility in Lawrenceville, Georgia;[1] followed by recording of specimens in an Enterprise Laboratory Information Management System (ELIMS)-compatible inventory spreadsheet.
- Engaging CDC laboratory staff and stakeholders in discussions about laboratory safety. LSIW has held 12 staff engagement sessions and has piloted peer-to-peer consultations at two laboratories. The workgroup has also conducted a laboratory staff survey and created a CDC Laboratory Safety intranet website that includes a Lab Safety Mailbox that is monitored daily. All staff who responded to a laboratory staff survey (which had an 82% response) agreed that the laboratory engagement sessions had allowed them to share ideas and solutions.
- Providing recommendations to the CDC Director. In a report issued on October 29th, the LSIW recommended that the CDC Director create a new position in the office of the director (an Associate Director for Laboratory Science and Safety, ADLSS) that could serve as a single point of accountability for agency laboratory safety and biosecurity. The LSIW also made recommendations on seven functional areas regarding laboratory safety, including Leadership, Staffing, and Organizational Structure; Training and Education; Policy, Authority, and Enforcement; Process and Standard Operating Procedures; Facilities, Systems, and Software; Communications; and Staff Feedback.

The LSIW also revised CDC's procedures for notifying management of laboratory incidents and potential exposures, and developed a standardized process for submitting and reviewing laboratory protocols for transferring inactivated and live materials from one laboratory to another. The process requires secondary verification of major steps in each transfer protocol, to be achieved through one of the methods approved by the CDC Director (e.g., verification via a camera recording, a centrifugal filtration device that indicates when filtration is complete). The LSIW proposed that an institutional protocol review board be established to oversee protocol reviews for laboratory safety.

[1]The repository in Lawrenceville is the CDC and ATSDR Specimen Packaging, Inventory, and Repository (CASPIR).

Phase II of LSIW activities will include expansion of biosafety training, under the auspices of a new CDC Biosafety Training Working Group that includes representatives from the Environment, Safety, and Health Compliance Office (ESHCO); the Center for Surveillance, Epidemiology and Laboratory Services (CSELS); and other CDC Centers. CDC will also pilot a Biological Risk Assessment Course for principal investigators, starting in February. Phase II will also include further implementation of secondary verification methods. Thus far, 35 out of 59 laboratories have elected to install cameras.

BSC Comments and Discussion

- An external Laboratory Safety Workgroup of the CDC Advisory Committee to the Director has also been formed to review laboratory safety practices at CDC as well as at NIH and FDA.
- Lessons learned by CDC on laboratory safety may also be useful to other institutions
- In response to a question about the costs associated with laboratory safety enhancements and audits of new systems (e.g., for inventory management), Dr. Dauphin said that CDC has budgeted for some of these initial improvements and that each enhancement includes an evaluation component
- In response to a question about the scope of the laboratory safety activities, Dr. Dauphin emphasized that while the first priority is to address biohazards at infectious disease laboratories, the new ADLSS will be responsible for safety issues across the agency, including those related to chemicals and radiation
- In response to a question about staff engagement efforts, Dr. Dauphin said that some staff have commented that the reviews required for lifting the moratoriums had actually helped improve morale by providing opportunities for laboratory staff to speak up and suggest improvements.
- In response to a question about unintended consequences
  - Dr. Khabbaz said that devoting more resources to laboratory safety may impact the pace of laboratory work, requiring CDC to prioritize laboratory activities. However, it is critical that CDC improve its quality management process to ensure laboratory safety.
  - Michael Shaw, OID Senior Advisor for Laboratory Science, said that much groundwork had already been laid before the recent laboratory incidents—especially regarding quality management and specimen inventories—but various constraints had slowed implementation. After the laboratory incidents, CDC reassessed its priorities and put more resources into laboratory safety. Steve Monroe, Deputy Director, NCEZID, said that the LSIW had to prioritize its moratorium reviews, based on which laboratories most urgently needed to resume operations. For example, the Ebola laboratory needed to provide outbreak support; the TB laboratory needed to continue work that affects management of patients with multidrug-resistant (MDR) TB; and the smallpox laboratory needed to test specimen vials labeled "variola" that had been found in an FDA storage room at NIH.
- In response to a question about dual-use research, Dr. Monroe, who serves as Chair of the CDC board that reviews dual-use projects, provided the following information:
  - No dual-use work is currently under way at CDC
  - CDC is updating its dual-use policy and incorporating questions on dual-use into the CDC electronic system for document clearance
  - CDC is also participating in a federal advisory panel charged with reviewing select agent rules and providing recommendations to OSTP
- Dr. Berkelman added that the National Academy of Science is holding a public meeting next week on gain-of-function dual-use research.

➢ **Report of the Antimicrobial Resistance Working Group**

Bob Weinstein, Co-Chair of the ARWG, reported on the group's December 8 meeting, which included discussions on the following topics:

- *National Strategy to Combat Antibiotic-Resistant Bacteria*.[2] The 5-year *CARB Strategy* was released in September along with an Executive Order. The goals of the Strategy include
  - Slowing the emergence and preventing the spread of AR
  - Strengthening One-Health surveillance
  - Developing rapid and innovative diagnostic tests
  - Accelerating development of new antibiotics and vaccines
  - Improving international collaboration to combat AR

  The Executive Order established a CARB Task Force, co-chaired by Secretaries of Defense, Agriculture, and HHS, that is charged with developing a National Action Plan to implement the Strategy and address the recommendation in the PCAST report on antimicrobial resistance.

  The AR Workgroup recommends that the CARB Action Plan include 1) time-phased measurable outputs to monitor progress in addressing the five CARB goals, as in the *HHS Action Plan to Prevent Healthcare-Associated Infections*; and 2) behavioral aspects of AR prevention activities (e.g., improved prescribing).

- Updates were provided on the following
  - The Council of State and Territorial Epidemiologists (CSTE) AR Task Force. This task force was established to identify solutions to improve AR surveillance, and includes four workgroups: Laboratory Testing, Data Reporting, Use of Data, and Public Health Research.
  - The Clinical and Laboratory Standards Institute (CSLI) Subcommittee on Susceptibility Testing. This subcommittee has been reorganized to streamline and prioritize work and also has four workgroups: Texts and Tables, Breakpoints, Quality Control, and Methodology.

- Prizes for AR Diagnostic Tests
  - NIH and BARDA will co-sponsor a $20M prize for development of rapid, diagnostic tests. An announcement will be posted in the *Federal Register* in early 2015 requesting input on test specifications (e.g., in terms of intended use, speed, costs, and technical characteristics).
  - Innovate UK (the Technical Strategy Board of the Government of the United Kingdom) has issued a Longitude Prize (https://longitudeprize.org/prize) to "create a cost-effective, accurate, rapid, and easy-to-use test for bacterial infections to allow healthcare providers worldwide to administer the right antibiotics at the right time."

  The ARWG emphasized that these prizes may significantly advance AR-related diagnostics and improve antibiotic use and that the availability of the new tests may also spur behavioral changes by healthcare providers and the public. More effective health communications is needed on AR and on long-term sustainability of changes in AR use. An update on the prizes will be provided at the ARWG meeting in May.

Dr. Weinstein also reported on Workgroup discussions regarding three focus areas:

1. **Laboratory Focus Area**. In considering this focus area, the ARWG assessed
- Gaps in AR testing performed in hospitals and testing needed for public health purposes. The Workgroup concluded that
  - Hospitals rarely test for resistance mechanisms
  - Many hospitals do not perform testing to detect colonization with MDR pathogens
  - Hospitals rarely perform typing studies to help characterize outbreaks
  - Hospitals rarely have the capacity to test new, recently approved drugs

[2] The *CARB Strategy* incorporates the categorization of AR threats outlined by the BSC ARWG.

- Gaps in use of whole genome sequencing (WGS) to identify resistance and susceptibility. The Workgroup concluded that
  - Use of WGS for clinical decision-making is very limited, in spite of tremendous advances. WGS has become relatively fast and cheap and has demonstrated utility for public health (e.g., for characterization of outbreak strains and evaluation of microbial transmission dynamics).
  - Improved bioinformatic tools are needed to interpret genomic data (e.g., to predict drug susceptibilities or other functions)

For this focus area, the Workgroup concluded that
- Periodic surveillance of resistance mechanisms for CRE and other pathogens would be helpful for infection control, treatment decisions, and epidemiologic studies
- Improved detection of colonization would be helpful for infection control (especially for emerging resistant pathogens)
- Testing and surveillance for resistance mechanisms is best achieved through regional reference laboratories.

2. **Prevention Focus Area.** In regard to regional AR prevention programs, the Workgroup concluded that ongoing evaluation of regional patterns and trends in AR spread can help provide
- A better understanding of AR drivers. This requires analysis of
  - Patterns of inpatient antibiotic prescribing (e.g., in different states or localities)
  - Patterns of healthcare access and utilization of services (e.g., dialysis)
  - Socio-economic drivers of AR spread
- Insight into emerging AR problems (i.e., by providing early warning that AR infections are likely to spread from one neighborhood or region to another)

Examples of regional AR surveillance systems include
- SENTRY, initiated in 1997 to monitor antimicrobial resistance on a global basis, using validated, reference-quality testing methods performed in a central laboratory (http://www.ncbi.nlm.nih.gov/pubmed/12807276)
- Surveillance Network-USA (TSN), managed by Eurofins Medine, in association with the Center for Disease Dynamics, Economics, and Policy, collects susceptibility test results from 300 clinical laboratories selected to be demographically representative of nine U.S. regions (http://www.eurofins.in/pharma/laboratory-testing-capabilities/global-infectious-disease-services/the-surveillance-network.aspx)
- European Centre for Disease Prevention and Control's (ECDC) antimicrobial resistance interactive database (EARS-Net), which collects information on the spread of antimicrobial resistance in Europe (http://www.ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx)

The Workgroup proposed seven core elements for CDC-supported Regional Prevent Programs:

Leadership. This element requires engagement of local opinion leaders and representatives of quality improvement organizations, health departments, long-term care facilities, and implementers of the Affordable Care Act.

Enhanced response activity. This element requires provision of expertise and technical assistance on outbreak control and disease prevention to acute care hospitals, long-term care facilities, and skilled nursing facilities.

Solidify laboratory capacity. This element requires enhancement of clinical laboratory practice and regional laboratory capacity to ensure reliable, accurate, and timely AR reporting.

Surveillance capacity. This element requires maximized use of existing NHSN data and near-horizon data; augmentation of these data to fill gaps; and improved technical expertise in analytics and informatics.

Educational Program

Communications Network. This element requires improved coordination of AR prevention efforts across the spectrum of regional healthcare organizations to address emerging (and spreading) threats.

Long-term prevention initiative. This element requires promotion of best practices for antibiotic stewardship.

As an example, Dr. Weinstein described regional carbapenem-resistant enterobacteriaceae (CRE) prevention activities in Illinois, which include establishment of a state-wide CRE Prevention Task Force; a CRE Detect and Protect Campaign, with webinars and resource packets; an extremely drug-resistant organism (XDRO) Registry for state-mandated CRE reporting (https://www.xdro.org/); and targeted interventions to prevent transmission of AR pathogens from long- term acute care hospitals to acute care hospitals and skilled nursing facilities.

The Workgroup suggested that

- Geographic data on resistance patterns and antibiotic use can help drive and direct establishment of prevention programs
- Active engagement and leadership by state and local health departments is critical to success
- Public recognition of hospitals for AR prevention efforts may be a useful incentive
- When the Ebola response is over, it would be good to channel momentum and lessons learned about the establishment of Ebola treatment centers in U.S. hospitals to AR prevention.

3. **Antibiotic Stewardship Focus Area.** The Workgroup discussed several topics related to advancing antibiotic stewardship to improve antibiotic use in inpatient settings, including

- Centers for Medicare and Medicaid Services (CMS) requirements that make antibiotic stewardship a requirement for Medicare-eligible hospitals by 2017
- An NHSN 2015 survey of ~4,000 hospitals that will include detailed questions on stewardship programs
- The need to increase surveillance for antibiotic use (AU) reporting to NHSN. So far, only about 60 hospitals are enrolled in the new NHSN AU module
- A new edition of EPIC software that is used in many hospitals is compatible with this module
- The benefits of developing an AU reporting measure for endorsement by the National Quality Forum (NQF). As part of this effort, CDC is planning an AU survey of 100 hospitals to provide a national "AU" snapshot.

The Workgroup advises that future CDC work in this area should

- Ensure that long-term care facilities use the NHSN AU module and develop antibiotic stewardship programs
- Include identification and analysis of additional data sources of AU data

The ARWG also advises that CDC set a national goal for reduction in outpatient antibiotic prescribing, using the following steps:

- **Establish a baseline for outpatient prescribing.** This activity will make use of data collected between 2008 and 2011 by the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS) on antibiotic use in physicians' offices and emergency departments. CDC will collaborate with partners at the University of Utah to determine antibiotic use by age, diagnosis, and antibiotic choice.

- **Convene an expert panel.** An initial meeting is tentatively planned for March 2015, with support from the Pew Charitable Trusts and facilitation from CDC. Participants will include representatives from stakeholder groups with expertise in outpatient antibiotic prescribing and/or stewardship to
  - Review existing data/guidelines for treatment of common infections
  - Determine recommended reductions in prescribing for each major diagnosis
  - Use Step 1 findings to inform next steps and define a process for establishing the goal
- **Establish a national goal**. The tentative plan is to
  - Set a threshold for how much antibiotic prescribing is appropriate for common infections that sometimes or rarely require antibiotic treatment
  - Compare this threshold with the actual percentage of visits that lead to prescriptions for antibiotics
  - Determine how great a reduction could be achieved for each common infection
  - Calculate an ideal population-based prescribing rate, based on achievable reductions for common infections. This rate would become the national goal.

  Once a national goal is established, CDC and partners will engage professional associations and advocacy groups to promote and support the national goal; issue reports for policymakers and scientific audiences; track progress toward achieving the national goal; and make adjustments as needed.

Next Steps. The AR Workgroup plans to hold conference calls every 2 months for each of the three Focus areas to discuss questions provided by CDC. The next in-person meeting is planned for May.

BSC Comments and Discussion

Laboratory Testing

- Point-of-care tests that allow faster and cheaper identification of MRSA and other AR pathogens would be very useful. Specimens are expensive to collect and the laboratory-testing process can be onerous. Diagnostic tests created in response to the U.S. and U.K. prizes could be game-changers.
- Culture testing will remain important in infectious disease research, and AR surveillance will continue to require tests that can detect resistance elements.
- It is difficult to create an assay for inpatient screening that covers the range of bacterial strains with different carbapenemases. Some diagnostic companies are looking for a single target that could capture all of them.
- Home-testing would be a valuable way to improve detection of resistant strains of strep, influenza, and pharyngitis. A patient might take a throat swab and test it at home; alternatively, the patient could bring the swab to a pharmacy or urgent care center, with no appointment necessary. When a result is positive, the patient could receive a prescription over the phone. In that case, the estimated 16% rate of antibiotic prescribing for adult patients with viral sore throats could be greatly reduced.

Regional AR Prevention

The ARWG might expand its scope to include

- Regional efforts to prevent community-acquired infections (e.g., infections with gonorrhea or TB).
- Resistance to antiviral drugs, which is likely to increase as more people receive treatment for hepatitis C virus and post-exposure prophylaxis for HIV. Thus far, the Workgroup briefly considered resistance to neuraminidase for treatment of influenza.

Antimicrobial Stewardship

- The CMS approach to strengthening stewardship may be very effective, if it is strong
- More focus is needed on outpatient prescribing practices–at both physician's offices and retail pharmacies
- Patients should be better educated about the potential harms of taking antibiotics when they are not needed

Next Steps. The BSC members agreed that the ARWG should continue, though additional members may be needed to address specific topics such as

- The need for research to better understand what drives consumer behavior related to use of antibiotics (and also vaccines).
- Whether additional guidelines, checklists, or HEDIS measures could help change antibiotic prescribing practices.
- Advice to CDC on best use of
  - Additional AR research funds that might become available to implement the CARB Strategy
  - New multiplex assays for foodborne diseases, assuming that they are validated and appropriate for public health use

➢ **Report of the Food Safety Modernization Act Surveillance Working Group**

Harry Chen, Chair of the FSMA SWG, reported on the group's December 8-9 meeting and presented the highlights of the FY 2014 Annual Report to the HHS Secretary.

Background. The FSMA SWG, established in 2011, is charged through FSMA with providing advice and recommendations to CDC and FDA (and through them to HHS) on criteria for the designation of Integrated Food Safety Centers of Excellence (submitted in 2012) and improvement of foodborne illness surveillance. The Working Group includes 21 members representing the BSC, CDC, USDA, FDA, academia, consumer groups, industry, and state and local health organizations. Six new members joined this year:

- Natalie Adan, Georgia Department of Agriculture
- Michael P. Doyle, University of Georgia
- Scott K. Hood, General Mills
- Elaine Scallan, University of Colorado, Denver
- Nathaniel H. Smith, Arkansas Department of Health
- Chris Waldrop, Consumer Federation of America

FSMA December 8-9 Meeting. The following topics were addressed at the FSMA SWG meeting:

- **Initiatives to improve interagency coordination and integrations**

  - The **Interagency Food Safety Analytics Collaboration (IFSAC)**, a joint effort by FDA's Center for Food Safety and Applied Nutrition (CFSAN), USDA's Food Safety and Inspection Service (FSIS), and CDC's Division of Foodborne, Waterborne, and Environmental Diseases (DFWED) to improve coordination of federal food-safety analytic efforts and address cross-cutting priorities for food safety data collection, analysis, and use. The IFSAC Strategic Plan for 2012-17 focuses on four foodborne pathogens: *Campylobacter, Listeria, Salmonella,* and STEC O157 (http://www.cdc.gov/foodsafety/ifsac/overview/strategic-plan.html). As part of these efforts, IFSAC has developed a new food categorization scheme to increase the accuracy and utility of

the food categories used to describe foods implicated in outbreaks and to generate foodborne illness source attribution estimates.

Feedback on IFSAC. The Working Group agreed that it is important to promote the visibility of IFSAC to industry, regulatory agencies, and consumer groups (e.g., via data-sharing), who can help advance AR surveillance activities, such as

- Integration of data to identify factors that contribute to foodborne outbreaks, including environmental antecedents, to better characterize outbreak causation
- Evaluation of interactions between organisms and foods, to identify food vehicles that are likely or unlikely to cause outbreaks and to frame attribution models
- Use of industry data, including food testing and environmental testing data, for food-safety research
- Evaluation of data on sporadic cases of foodborne disease, using case-control studies and laboratory methods such as WGS to learn more about attribution and about the relationship between sporadic cases and outbreaks

- **The Interagency Foodborne Outbreak Response Collaboration (IFORC)**, which develops and coordinates federal best practices for detection of foodborne outbreaks; generation and testing of hypotheses about outbreak causation, with input from industry partners; identification of food vehicles for outbreak-causing microbes; enhancement of data sharing and analyses; and development of interagency and public health communication strategies and processes.

  Feedback on IFORC. The Working Group agreed that IFORC can help advance
  - Coordinated messaging and timing with state and local health departments
  - Education of the public and media about the science behind outbreak processes
  - Promotion of transparency and consistency in the decision making process
  - Inclusion of states officials and industry partners in discussions about lessons learned during outbreaks so that future outbreaks can be prevented
  - Creation of metrics to evaluate the success of the interagency collaboration

- **Multi-Agency WGS collaborations**, such as the *Listeria* WGS surveillance project**.** Multi-agency collaborations can improve outbreak detection and investigation, make information on attribution, virulence, and resistance available more quickly, and enhance analyses of resistance trends. They can also advance
  - Development of a practical system for local, national, and global WGS data-sharing, data analysis, and communication
  - Adaptation of public health practices to changing clinical diagnostics (e.g., use of culture-independent diagnostic tests).

  Feedback on Multi-Agency WGS Collaborations. The Workgroup recognizes that significant progress has been made in this area over a short period of time. Multi-agency WGS collaborations can help
  - Standardize sequencing methodology across federal agencies
  - Create a uniform platform that provides standardized nomenclature for identifying pathogen strains
  - Provide an implementation toolkit for the adoption of WGS in industry. These efforts may be advanced through collaboration with the Council to Improve Foodborne Outbreak Response **(**CIFOR) Industry Guidelines Workgroup, which is developing response guidelines to help industry in day-to-day operations and during investigations of foodborne illness outbreaks. (CIFOR is discussed further below.)

- **Collaborations with State and Local Partners**

  Updates were provided on
  - **Integrated Food Safety Centers of Excellence (COEs)**, which were established as an FSMA requirement to "serve as resources for federal, state, and local public health professionals to respond to foodborne illness outbreaks." The COEs, which are located at state health departments in Colorado, Florida, Minnesota, Oregon, and Tennessee, partner with academic institutions.
  - **CIFOR**, co-chaired by CSTE and NACCHO, a multi-disciplinary work group formed in 2006 that includes representatives from federal agencies and national professional organizations.
  - **Foodborne Disease Centers for Outbreak Response Enhancement (FoodCORE**), which aims to improve detection, investigation and control of foodborne outbreaks. The FoodCORE Centers—located in Connecticut, Colorado, Minnesota, New York City, Ohio, Oregon, South Carolina, Tennessee, Utah, and Wisconsin—work together to test innovative methods, share strategies, and identify and document model practices.

    Feedback on FoodCORE. The Workgroup agreed that FoodCORE
    - Is a relatively inexpensive, sustainable investment that provides a vision for a national program to improve detection, investigation, and control of foodborne disease outbreaks
    - Should be expanded nationally, through public health investment in the 40 states that do not currently host FoodCORE sites
    - Provides surge capacity that goes beyond foodborne outbreaks, as demonstrated by FoodCore's assistance with the Ebola response in Ohio and New York City
    - Should use core measures developed by CIFOR to identify target goals and measure progress in achieving them

- **Enhanced Surveillance Tools**

  - **Improved surveillance for cyclosporiasis**, which is currently conducted by the Nationally Notifiable Disease Surveillance System (NNDSS), with trends monitored by the 10 FoodNET sites. Cyclosporiais is currently a reportable disease in 40 states.

    The recent outbreak of cyclosporiasis—which was traced to contaminated cilantro imported from Mexico—involved 345 confirmed cases, including 235 cases with no history of international travel. The nontravel cases were reported by 22 states and New York City, with 57% reported by Texas.

    During FY 2015, CDC will explore research options for improving surveillance and reducing outbreaks, and FDA will continue to work with the Mexican National Service for Agro-Alimentary Public Health, Safety and Quality (SENASICA) and the Federal Commission for the Protection from Sanitary Risks (COFEPRIS) to promote the safety of fresh and minimally processed agricultural products through a Produce Safety Partnership.

    Feedback on Surveillance for Cyclosporiasis. The Working Group suggests that additional efforts are needed to
    - Educate providers about identifying cases and ordering proper diagnostic laboratory tests
    - Improve reporting of cases to federal agencies, using electronic reporting systems
    - Modernize laboratory methods to improve identification of illness
    - Focus on regulatory relationship with Mexico and other source countries

- **Use of *System for Enteric Disease Response, Investigation, and Coordination* (SEDRIC)** software to facilitate tracking of foodborne diseases during multistate outbreaks. SEDRIC was developed by CDC and Palantir Technologies to integrate data from different sources in real time; facilitate epidemiologic, laboratory, and traceback activities; facilitate data visualization; and enable secure information sharing among state, local, and federal partners.

  Feedback on SEDRIC. The Working Group agreed that while the technology is in its infancy SEDRIC has the potential to
  - Provide flexibility and security in sharing information with states and partners
  - Help assess outbreak metrics (e.g., timeliness, completeness)
  - Develop a resource base in anticipation of WGS to make decisions about which clusters to investigate and when

Next Steps. Potential topics for the FSMA Working Group during 2015 include
- Environmental risk factors and antecedents of foodborne disease outbreaks
- Updates on *Vibrio* infection, considered as a neglected disease

FSMA SWG Annual Report

Two key topics were addressed in the FSMA SWG annual report for 2014: 1) enhancing surveillance for foodborne illness and outbreaks caused by norovirus and 2) enhancing antimicrobial resistance surveillance for foodborne illnesses.

1. Enhancing surveillance for foodborne illness and outbreaks caused by norovirus

The Workgroup agreed on the following:
- Support should be provided to state and local authorities for training and education on the importance of surveillance for foodborne norovirus; increased reporting of norovirus illnesses; and development of standardized outbreak investigation and reporting protocols
- Measures to strengthen existing national surveillance tools and systems (i.e., NORS and CaliciNet) should be continued and sustained
- Targeted studies should be conducted to evaluate the role/utility of sentinel surveillance sites in a few states (via NoroSTAT), including complaint-based surveillance and syndromic surveillance
- Focused studies on norovirus transmission are also needed, including
  - Environmental assessments to identify points in the food chain at which a product may be contaminated (i.e., production, manufacturing, food handling); the proportion of contamination that occurs pre-retail; and the role of aerosolization of vomitus in contamination of foods
  - Epidemiologic attribution studies to learn more about sources of norovirus contamination of foods, especially for outbreaks involving more than one contaminated food product
  - Intensive investigation of outbreaks in high-risk settings to identify contributing factors and potential control measures
- Routine testing of foods for norovirus contamination is currently not feasible or advisable
- Continued research is needed to develop and license sanitizers, disinfectants, and vaccines with established efficacy to control norovirus. As these products develop, further study will be necessary to identify specific risk groups to target for these prevention and control efforts.

2. Enhancing antimicrobial resistance surveillance for foodborne illnesses

The Working Group agreed that the National Antimicrobial Resistance Monitoring System (NARMS) should be enhanced by

- Providing standardized definitions for antimicrobial resistance and identifying new sources of data
- Increasing the sample sizes of retail meat specimens and bacterial strains isolated from patients
- Collecting additional data on patient exposures (e.g., involving food or travel)
- Comparing AR information on outbreak strain isolates with NARMS susceptibility testing data
- Enhancing linkage of NARMS to other databases related to foodborne diseases (e.g., NORS, FoodNet, and PulseNet)
- Collecting and linking environmental health information with NARMS data
- Conducting epidemiologic studies that meet the needs of stakeholders
- Collecting and linking additional environmental health information to NARMS data
- Increasing use of WGS, as resources allow
- Continuing to augment collaborations among federal agencies and with state partners, private healthcare systems, industry, and other stakeholders

To implement these improvements, CDC and partners can

- Explore new sources of and resource requirements for the collection of clinical and antimicrobial susceptibility data
- Explore how primary antimicrobial susceptibility testing could be best conducted at the state or clinical laboratory level, with results forward to CDC for analysis and distribution
- Increase WGS with accompanying phenotypic and epidemiologic information on isolates to use in comparisons and linkages between environmental, food, and clinical outbreak isolates
- Explore how antimicrobial susceptibility testing could be conducted in food production animals at the preharvest/on-the-farm level

In addition, the FSMA SWG

- Encourages the use of AR data to ensure that messaging is focused on providing information for decision making, identify different stakeholders and tailoring reports to their needs, and provide reports on a quicker timeline, balancing the need to "go live" with time needed to obtain information for annual reports
- Agrees that sharing and utilizing human antimicrobial resistance data with international partners, based on standardized methods and reporting, is essential for effectively confronting this growing global problem
- Encourages collaborations and partnerships with WHO, Canada and Europe

The BSC members voted to accept the 2014 FSMA SWG annual report, which will be submitted to the HHS Secretary in January.

BSC Comments and Discussion

Data-Sharing

- CDC partners would benefit from more rapid and timely sharing of surveillance data
- The AR Annual Report, *Vital Signs* articles, and other CDC publications often make use of annual data sets that are one or more years old. This lag represents the time needed to gain data-sharing permission from partners, to analyze and validate the data, and to obtain agency-wide clearance. Quick-posting of data is typically only achieved during outbreaks.
- Dr. Khabbaz noted that data-sharing issues go beyond food safety data and that achieving more rapid and granular access to all disease data collected by CDC is a priority for the CDC Director.

- In the future, SEDRIC may provide a vehicle for making data rapidly available to response partners.

Norovirus

- In response to a question about using molecular tools to track norovirus, Dr. Chen said that CaliciNET allows subtyping and might be used like PulseNET to identify and monitor outbreaks. Thus far, CaliciNET's primary use has been in conducting retrospective studies.
- In response to questions about vaccine development, CDC program staff indicated that current vaccine candidates are in different developmental phases. The one that is furthest along is expected to undergo phase III trials in 2015, with possible licensing in 2018. Thus far, its efficacy appears to be moderate.

NARMS

- In response to a question about NARMS, Chris Braden, DFWED Director, explained that NARMS data are collected at sentinel sites (i.e., the 10 FoodNET sites). Increased resources would enable additional testing for antimicrobial resistance, with greater geographical scope and granularity.

➢ **Report of the Infectious Disease Laboratory Working Group (IDLWG)**

Jill Taylor, IDLWG Co-Chair, reported on the group's December 8 meeting, which focused on several advanced molecular detection (AMD) topics:

Recent AMD Applications

- **International outbreak of MERS-CoV.** CDC sequenced the genomes of viruses isolated from two U.S travel-related cases of MERS-CoV and determined that they were similar to other known viral isolates.
- **Outbreak of hepatitis A in pomegranates, affecting 10 states**. WGS was used to trace the virus to contaminated pomegranate seeds from Turkey; FDA worked with the company selling the seeds to ensure that no additional contaminated shipments were sold.
- **Ebola outbreak in West Africa**. Genetic sequencing of viruses isolated from Ebola patients hospitalized in the United States, indicated that the strains were 97% similar to those isolated during the 1976 outbreak in Zaire (now the Democratic Republic of the Congo).
- **U.S. outbreak of Enterovirus D-68 Infections**. CDC submitted genomic sequences to GenBank and developed a PCR assay that was provided to public health laboratories.

AMD Funding and Resources. FY 2014 AMD resources were used to support

- Improvements in IT infrastructure, including increased data storage and establishment of a network for high performance computing.
  - CDC has doubled the number of laboratories with access to next generation sequencing (NGS) core facility
  - In the future, CDC may utilize cloud storage
  - With hardware in place, CDC is now focusing on increasing expertise in bioinformatics
- Coordination of AMD across the agency, using a hybrid approach that combines development of common systems with efforts to address individualized needs
- Major sequencing efforts in many infectious disease areas, including projects to transition laboratory programs from traditional to NGS diagnostic techniques, as well as exploratory, cutting-edge projects to further advance the use of such techniques

- Collaborations with Georgia Tech to provide classes in bioinformatics and establish the APHL Bioinformatics Fellowship Program, which is modeled after the Emerging Infectious Diseases (EID) Laboratory Fellowship Program

FY14 AMD Projects. 24 CDC AMD projects were funded, including a cross-cutting project on metagenomics and a project to advance use of AMD techniques at EIP sites. Other projects included
- Using NGS studies to better understand and intervene in tuberculosis outbreaks through rapid AR characterization of outbreak strains
- Modernizing our approach to identification of unknown respiratory disease outbreaks
- Using NGS sequencing tools to detect drug-resistant malaria

In accord with guidance provided by IDLWG and the BSC last May, CDC allocated $2 million in FY14 funds to advance AMD activities at state public health laboratories. Support was provided for AMD training (via the Epidemiology and Laboratory Capacity [ELC] program) and for participation in the interagency NGS *Listeria* Surveillance Project (page 2); the Cyclosporoisis Surveillance Project, which uses WGS; and the Unexplained Respiratory Disease Outbreaks, which uses metagenomic techniques.

AMD Metrics: How to Demonstrate Success? Examples of AMD metrics used by CDC include
- Increases in the number of specimens analyzed by NGS, including the number of influenza strains characterized by WGS to help inform vaccine selection
- Diagnostic value of AMD techniques (i.e., in terms of faster results and more detailed information)
- Cost-savings to CDC due to replacement of traditional methods with NGS
- Cost-savings to the U.S. healthcare system, due to more rapid detection and control of outbreaks

CDC is continuing to consider the best metrics for measuring AMD progress and is working towards having all laboratories move in the same direction and use the same metrics.

FY 2015 Intramural Funds. FY 2015 AMD funds will support renewals of 21 FY 2014 AMD projects ($8-$9M); new "incubator projects," which are intended to be more exploratory and cutting-edge ($1M); and new "ready-to-go" projects ($2-$3M).

Reaching Out: Collaborations
- Responses to CDC's "No Petri Dish challenge" applications are under review
- Ongoing partnerships include
  - Industry partnerships with TGen, the Broad Institute, and the Welcome Trust Sanger Institute
  - Interagency partnerships with FDA, NIH, USDA, and DoD
  - Academic partnerships with Georgia Tech, Emory University, and University of California, Davis
  - CDC is also working with APHL, to evaluate state AMD capacities and develop an AMD roadmap for public health laboratories

Data-Sharing Issues. CDC and partners are considering how to address social and technical obstacles to sharing sequence data and related metadata. Issues include sharing data across jurisdictions and preserving privacy and confidentiality. For the most part, these issues are currently resolved on a case-by-case basis.

Feedback and Direction from the IDLWG

The ID Lab WG noted that
- CDC has made good progress in the first year of the AMD initiative
- Staying on track will require
  - Constant re-evaluations
  - Maintaining a good balance between traditional and molecular diagnostic techniques

  - Developing and implementing quality control and quality assurance standards
- CDC should develop a long-term (5-10 year) AMD plan to address
  - Development and dissemination of metrics
  - Quality assurance and quality control issues
  - Advancement of "positive health economics" by demonstrating the clinical and public health value of AMD diagnostics, in terms of improved health and reduced costs
- The CDC Working Group on Quality Assurance and Quality Control should work with FDA, NIH, state health departments, and other partners to develop
  - Standardized protocols that can be applied across studies using different types of specimens and different sequencing equipment
  - Guidelines on how to interpret the WGS and metagenomic data for public health purposes, analogous to the guidelines currently used to interpret PFGE data

The IDLWG discussed whether it can best help advance AMD activities at CDC by
- Focusing on few AMD projects to gain a better understanding of the process (with respect to both successes and challenges) or staying at a high level and reviewing all AMD projects
- Focusing on the overarching need for the AMD enterprise to demonstrate improved health economics as well as on laboratory issues

These issues require additional discussions.

The IDLWG also identified several gaps and topics needing additional consideration:
- Public health use of other diagnostic technologies, including digital PCR and MALDI-TOF technology
- Advancing the preparation of clinical samples for metagenomic analysis
- Addressing bioinformatics issues of importance to the public health community, including work force shortages and the need for common analysis "pipelines"
- Working with diagnostic-test manufacturers and clinical laboratories to develop diagnostics that will fulfill both clinical and public health needs. The diagnostic world is rapidly converting from culture-based diagnostics to "closed-system" tests (including point-of-care tests) that do not provide samples or sequencing data.

BSC Comments and Discussion

General Comments
- CDC should consider how the IDLWG may be of most help in advancing AMD goals
- All three BSC workgroups discussed issues related to antimicrobial resistance, AMD, and the need for harmonized data standards and improved data management. It is imperative that all public health scientists who work with bioinformatics and/or WGS "speak the same language."
- The overlap among the three working groups underscores the importance of these cross-cutting issues. The workgroup chairs should consider whether to hold combined meetings and whether to issue joint guidance and/or recommendations.

Big Data and Value
- In deciding which AMD projects to fund, it is important to consider the expected outcomes of the huge amount of sequencing data that the project will generate. WGS may help us identify resistant bacterial strains, and viral sequences may help us identify targets for antiviral drugs. However, it is difficult to know in advance which outcomes will be useful for public health purposes.
- These are difficult questions that don't yet have answers. Until we know more, it is important to build shared and well-curated databases of microbial genomic sequences and make sure that the data are valid, reproducible, and standardized.

CDC's Role

- It was suggested that CDC
  - Focus on what CDC does best and reach to others for what has been done elsewhere (e.g., at NIH and universities)
  - Continue to hold AMD seminars and invite the research community for discussions about using metagenomic techniques for public health purposes
  - Provide additional postdoctoral fellowships and grants to address specific public health issues

Duncan MacCannell, NCEZID Science Officer, noted that CDC is participating in informal "communities of practice" that share ideas and discuss technical issues about WGS and bioinformatics.

AMD at State Laboratories

- Although AMD activities hold great benefits for state laboratories, resources are a major issue. Each state laboratory cannot afford to purchase new equipment each time a better model comes on the market. It may be better to equip four or five state laboratories with state-of- the-art equipment. These issues will be discussed at the APHL/CDC meeting in February convened to develop an AMD roadmap.
- A type of "regionalization" is already happening, through the centers of excellence public health laboratories that address influenza, AR testing, and TB. However, if "desktop sequencing" technology becomes successful and cheap, the picture may change.
- Bioinformatics requires a different sort of regionalization–making resources available online rather than having a bioinformatics core in every laboratory

Communications and Education

- Common language is important not only among scientists, but also among politicians and healthcare providers. The goals and achievements of AMD must be explained clearly and succinctly. Education is also needed at many levels.
- This is an area where metrics will be very important. For example, CDC and partners should describe how sequencing a TB genome leads to rapid treatment of a patient.
- Standardization of language is important but not easy. It was suggested that this might be an area where the IDLWG might help.

➢ **Emerging Severe Viral Respiratory Disease (EV-D68 and MERS)—Update and Discussion**

Mark Pallansch, Director, NCIRD Division of Viral Diseases, reported on outbreaks of severe viral respiratory disease involving enterovirus D68 (EV-D68) in the United States and on Middle Eastern respiratory syndrome-coronavirus (MERS-CoV).

EV-D68 Dr. Pallansch noted that

- Enteroviruses are common viruses that cause 10-15 million symptomatic infections in the United States each year, mostly in the summer and fall, and mostly in children. Although most infected people are asymptomatic or have mild respiratory symptoms, some patients exhibit a febrile rash illness (e.g., hand, food, and mouth disease) and/or neurologic symptoms.
- Enterovirus infections are not nationally notifiable. Public health monitoring of enteroviruses is implemented through two passive laboratory-based surveillance systems: the National Respiratory and Enteric Virus Surveillance System (NREVSS) and the National Enterovirus Surveillance System (NESS).
- More than 100 different types of enteroviruses have been identified. EV-D68, which was first identified in 1962, belongs to a small set of enterviruses (the "D" enteroviruses) which so far includes

only 5 members that affect humans. EV-D68 is thought to occur less commonly than many other types of enteroviruses.

- EV-D68 causes respiratory illness in both children and adults, with symptoms similar to those caused by rhinoviruses. Since 2008, several small clusters have been described in Japan, China, the Philippines, the Netherlands, and the United States (in Georgia, Pennslyvania, and Arizona).

The first signal of a U.S. outbreak in 2014 came from NREVSS and NESS reports last summer that found

- Increases in severe respiratory illnesses among children admitted to hospitals and to pediatric intensive care units (PICUs) in several jurisdictions
- Increases in rhinovirus and enterovirus infections, as detected by multiplex PCR assays that do not distinguish between rhinoviruses and enteroviruses

During the late summer and fall, several states and large cities reported increases in acute respiratory illnesses as compared to previous years, with a significant rise in emergency department visits and hospitalizations. In September, EV-D68 outbreaks were reported in PICUs in Missouri and Illinois. Most of the affected children had a history of asthma or reactive airway disease, and many required mechanical ventilation. Only a minority of the cases involved fever.

Nationwide testing by CDC and state laboratories determined that about 36% of acute respiratory disease cases were positive for EV-D68, while about 33% tested positive for other viruses, including rhinoviruses, coxsackieviruses, and echoviruses. Thus far, EV-D68 has been detected in more than 1000 patient specimens from 48 states and the District of Columbia. Although 12 patients who died were positive for EV-D68, the role of the virus in these deaths is unclear and is still under investigation.

MERS-CoV

Outbreak in the Middle East

- Thus far, the MERS-CoV outbreak has involved 927 laboratory-confirmed cases. Although the case fatality rate is high (39%), some mild cases have occurred.
- The first case of MERS-CoV was reported in September 2012, and the most recent case was reported in November 2014 (both in Saudi Arabia). The disease has affected more males than females (579 males, 314 females, 34 unknown), with a median age of 48 years (range 0-99 yrs); 19% of the cases occurred in healthcare workers.
- Most cases occurred in 36 small clusters (in healthcare facilities and households), and all cases have an epidemiologic link to 9 countries: Saudi Arabia, Qatar, United Arab Emirates, Jordan, Yemen, Oman, Lebanon, Iran, and Kuwait.
- A significant increase in cases occurred in Saudi Arabia this past spring, and CDC sent a team to assist the Saudi Ministry of Health when a hospital outbreak occurred in October.

U.S. Cases of MERS-CoV. In the United States, CDC has tested about 500 patients for MERS-CoV, and 2 have tested positive, 1 in Indiana and 1 Florida. Both patients were travelers from Saudi Arabia.

Transmission of MERS-CoV.

- Person-to-person transmission of MERS-CoV is well documented, although the virus is less easily transmitted than the SARS virus. The median incubation period is just over 5 days, with a range of 2-14 days. Although routes of transmission are not fully understood, there is no clear evidence of sustained community transmission. A recent study of household transmission involving 26 index

patients and their 280 household contacts identified only 12 probable cases of secondary transmission (4%), which were related to only 6 of the 26 index patients (23%).[3]

- The spike in cases in Saudi Arabia last spring was due to disease clusters within healthcare facilities. Risk factors included underlying comorbidities and receiving care in a dialysis unit. Interventions included improved infection control trainings in healthcare settings.
- Efforts are underway to identify which exposures are most important for transmission, with special attention to healthcare exposures and animal exposures. Although MERS-CoV has been detected in camels, few if any patients have documented histories of exposure to these animals.
- Current response efforts include reviewing the seasonality of MER-CoV infections and their impact on vulnerable populations; advancing the development of vaccines and antivirals; and using AMD techniques to monitor changes in genomic sequences. However, lack of access to specimens continues to be a major roadblock.

BSC Comments and Discussion

Surveillance for Severe Respiratory Disease

- In regard to surveillance for severe respiratory disease, BSC members suggested that
  - It might be helpful to establish in-depth surveillance for EV-D68 at a few sentinel sites
  - Other sources of surveillance data might include Biosense and hospital admissions rates for acute respiratory disease. In some locations, those rates rose so dramatically in September that hospitals diverted patients to other hospitals, as they sometimes do during an influenza outbreak.
  - The Influenza Incidence Surveillance Project (IISP) and the Severe Acute Respiratory Infections (SARI) surveillance system in Minnesota might also provide useful data. These projects involve collecting swabs for all cases of influenza-like illness (ILI) and recording epidemiologic, clinical, and laboratory data associated with each swab. Out-of-season ICU admissions for ILI might also be a good surveillance indicator.
  - Nationwide, state-level surveillance for influenza might be scaled up to test for other respiratory and/or febrile diseases and using test panels and multiplex PCR assays.
- In regard to detection of the EV-D68 outbreak, Dr. Pallansch noted that increases in severe respiratory illness were detected through passive surveillance systems, and the impact of EV-D68 on a vulnerable group was evaluated during the investigation of the PICU outbreaks in Missouri and Illinois. Increases in respiratory disease were not detected through ILI surveillance, because only a minority of EV-D68 cases involved fever.

EV-D68

- In response to a question about testing for EV-D68, Dr. Pallansch noted that
  - Once it became clear that EV-D68 was the cause of the PICU outbreaks, that children with underlying disease were at highest risk, and that physicians were already doing what needed to be done, many states decided to stop testing. CDC then shifted its focus to investigating fatal cases and cases of paralytic disease.
  - CDC provided guidance to states that requested EV-D68 testing by CDC or that performed their own testing. CDC did not require states to test for EV-D68.
  - CDC developed an EV-D68-specific RT-rPCR assay and posted the protocol on the CDC website.
- Joint U.S.-Mexico border surveillance for infectious diseases has been in place for many years. As part of a joint U.S.-Mexico study, CDC is testing respiratory specimens collected over the past 4 years from children and adults in Mexico City. The aims of the study are to compare EV-D68 events in the U.S. and Mexico and begin to determine the range of respiratory viruses and the spectrum of severity of viral respiratory disease in the U.S., Mexico, and Canada.

[3] Drosten, et al. N Engl J Med 2014;371:828-35.

- In response to a question about molecular characterization of EV-D68, Dr. Pallansch stated that
  - Until recently, CDC had used sequencing data primarily for retrospective characterization of enteroviral strains. This year, CDC transitioned from using classic neutralization techniques to using NGS to identify strains.
  - The EV-D68 strain isolated in 2014 is the same as the strain isolated in 2012. Why the incidence rose this year remains a mystery. The epidemiology of enteroviruses has been unpredictable over the past 30 years, and there is no direct evidence that EV-D68 was causing significant human illness prior to 2012.
  - Thus far, no epidemiologic changes in EV-D68 (e.g., related to transmissibility or disease severity) have been correlated with genetic changes in the virus. However, the EV-D68 genome includes a single amino acid change that provides resistance to a class of antivirals called capsid inhibitors. EV-D68 is not susceptible to any candidate antiviral candidate drug tested by CDC.
  - CDC is considering how to use NGS to anticipate what might be expected next year. The current plan is to use the RT-rPCR assay to identify viruses that circulate during the earliest stage of the 2015 enterovirus season. However, previous studies suggest that this approach may have only about a 60% predictive value in predicting what the dominant strains will be over the course of the year.

MERS-CoV

- In response to a question about whether the seasonality of MERS-CoV could be related to viral shedding during the weaning of young camels, Dr. Pallansch said that an ecologic factor related to the camel lifecycle might be important, although proving it will be a challenge
- In regard to a question about infection control in Saudi hospitals, Dr. Pallansch reported that the Saudi Ministry of Health has implemented rapid triage, testing, and isolation of patients infected with MERS-CoV
- Dr. Berkelman noted that access to specimens has been an issue during the Ebola outbreak as well.

➢ CDC Response to the Ebola Outbreak—Update and Discussion

Beth Bell, NCEZID Director, provided the following updates:

Response to the Ebola Outbreak in West Africa

- The total number of cases of Ebola virus disease (EVD) in Guinea, Liberia, and Sierra Leone as of December 8 is 17,800 (of which 11,182 are laboratory confirmed) and the number of deaths is 6,331. The epidemic has been driven by unsafe care and unsafe burials, and the response strategy has therefore focused on ensuring adequate isolation and treatment capacity and changes in burial practices, as well as improved incident management, restoration of the healthcare system, and social mobilization and communication. Getting to zero will continue to require isolation and care, contact tracing, laboratory testing, and rapid response to hotspots.
- In Guinea, contact-tracing remains a priority, especially in the capital city of Conakry, and in forested areas where there has been poor acceptance of response efforts. In Liberia, the disease rate has flattened out, but not stopped. CDC is helping to advance response efforts at the district and sub-district levels, including rapid response to hot spots. In Sierra Leone, the disease rate continues to go up, due to the same issues responders wrestled with in Liberia–inadequate isolation facilities and laboratory capacity. Dr. Bell emphasized that we are at a critical point where it is clear what needs to be done and that we need to do it as fast as possible.
- CDC, WHO, and other international partners are assisting the Mali Ministry of Health in controlling a cluster of cases in Mali, where an imam from a border village traveled from Guinea to Mali and died in a hospital in Bamako from what was later recognized as Ebola.

- CDC is also working with research partners to advance the development of rapid tests and better personal protective equipment (PPE) and is actively involved in the design of vaccine trials.

Domestic Preparedness

- CDC is conducting entry screening and post-arrival monitoring of incoming travelers from affected countries and ensuring that selected U.S. healthcare facilities are ready to evaluate symptomatic travelers and provide treatment, as needed. To advance these efforts, CDC has provided key guidance documents, including "Monitoring and Movement" guidance that defines exposure risk categories, provides guidance on clinical criteria, and guidance on public health action (e.g., clinical evaluation, follow-up, and travel restrictions).
- CDC works closely with the Department of Homeland Security's (DHS) Customs and Border Protection agents, with airlines, and with emergency medical services to identify sick travelers with possible contagious diseases. To ensure detection of travel-related cases of Ebola, CDC is also working with DHS to conduct enhanced entry screening at the 5 U.S. airports where all U.S.-bound air travelers who have been in Guinea, Liberia, Sierra Leone, or Mali arrive. In addition to screening for risk and symptoms, these travelers receive a "Check and Report Ebola (CARE) Kit," which includes tools to help them check their temperature and watch for symptoms for 21 days, and information on whom to call if they develop symptoms.
- ***Post arrival monitoring.*** CDC securely transmits contact information on arriving passengers to the health department at the traveler's final destination. Subsequently, that health department monitors the traveler for 21 days after his or her departure date from the affected country. *Active monitoring* of those in the low but not zero risk category includes having the traveler report his or her temperature and symptoms (if any) twice a day by phone, with active follow-up of any non-responders. *Direct active monitoring* of those in "some" or "high risk" categories additionally involves daily visual contact with each traveler.
- ***Hospital preparedness***. CDC has also provided interim guidance for hospital preparedness that involves three "tiers" of hospitals: Ebola Treatment Centers (ETCs), which can care for and manage patients; Ebola Assessment Hospitals, which can evaluate and care for a patient for up to 96 hours or until the patient is transferred to an ETC; and Frontline Healthcare Facilities, which can safely identify and isolate patients with Ebola symptoms and histories of known or potential exposure. CDC conducts site visits of potential ETCs to assess and provide training regarding the hospital's infection control capacity, physical infrastructure, staffing resources, waste management processes, laboratory set-up, and supplies of PPE needed to provide safe care for Ebola patients. ETC staff must be trained in putting on and taking off PPE and in providing clinical care using PPE.
- CDC has answered more than 700 clinical inquiries from health departments and healthcare providers regarding persons potentially at risk for Ebola virus disease.
- ***Tools for Healthcare Workers***. CDC has also provided online tools for healthcare workers, including algorithms, checklists, videos, and audio podcasts, infographics, and slide sets. The development of these tools was informed by formative research conducted with stakeholders. Online training resources include PPE training videos—developed with Johns Hopkins University, Miami University, the Association for Professionals in Infection Control and Epidemiology (APIC), and the Society for Healthcare Epidemiology of America (SHEA)—as well as a shortened PPE demonstration video developed by MedScape. CDC has also conducted more than 130 webinars and conference calls (reaching over 150,000 people), and has conducted live training events in NYC and LA, in conjunction with the Partnership for Quality Care, hospital associations, and healthcare unions.

Dr. Bell reported that the emergency request to Congress for $1.8 billion to support the Ebola outbreak response includes funding for the international response in the three affected countries and in nearby countries at high risk; for domestic activities (e.g., state-level preparedness, laboratory capacity, infection control, and entry screening); and for the Global Heath Security Agenda to build public health capacity in

developing nations. Dr. Bell concluded by mentioning that *Time Magazine* has declared its 2014 Person of the Year to be "The Ebola Fighters."

BSC Comments and Discussion

Ebola Response Partnerships and Roles

- In response to a question about coordination in the field, Dr. Bell stated that the U.S. response in Liberia, Guinea and Sierra Leone is coordinated by USAID/OFDA Disaster Assistance Response Teams (DARTs), which include CDC members
- Médecins Sans Frontières (MSF) is playing a critical role in all countries, focusing on treatment of Ebola patients. However, a continuing challenge is lack of healthcare staff for ETUs. USAID, MSF, and other agencies have recruited a cadre of volunteers.
- The Ebola outbreak is a far bigger public health issue than any one organization can address. Jonathan Mermin, NCHHSTP Director, who recently returned from Sierra Leone, observed that collaboration among response partners in Sierra Leone (including all levels of the Government of Sierra Leone, NGOs, UK partners, USAID, and CDC) is excellent, because everyone recognizes what needs to be done and that more people are needed to do it. Sierra Leone is an extremely poor country whose healthcare and public health systems have been destroyed by civil war. Dr. Mermin compared the response to running a 100-yard dash in which the runner does not stop to breathe—although in duration the response is more like a marathon. However, the pace in Sierra Leone is getting less frantic because the number of cases is declining in neighborhoods that had experienced massive epidemics. The local people are learning what to do to protect themselves and their families.
- Dramatic improvement is possible over the next 3 months—as long as the epidemic does not spread to other parts of Africa or to another continent.

Public Health Data

- Another response issue involves the challenges in collecting comprehensive epidemiologic data to guide the response (e.g., to explain why the incidence of Ebola has gone up or down in different localities)
- Dr. Bell noted that CDC has regularly consulted with Team B, a CDC-convened group of outside experts, including experts in filoviruses, on scientific issues such as risk of viral mutation
- Regarding collection of data on child health, Dr. Bell noted that disruption in routine childhood services has made local healthcare capacity for children even weaker than when the epidemic started. It is important to characterize these secondary effects by capturing data on vaccine rates, under-five mortality, and the number of new orphans.

Domestic Preparedness

- In response to a question about whether people entering the United States from affected countries can circumvent the tracking system, Dr. Bell noted that the system is working well, with individuals checking in every day. The process begins with entry screening when the individual enters the country. CDC then notifies the health department in the state or large city that will be the person's final destination. Thus far, health departments are in contact with 99% of people participating in the program.
- Some states have adopted monitoring standards and procedures that are more stringent than those recommended by CDC. For example, some are issuing quarantine orders or restricting travel by public conveyance.

Emergency Response Funds

- The domestic emergency response funds will focus on preparedness, laboratory safety, infection control, entry screening, and post-arrival monitoring. Globally, the funds will be used to stop the

outbreak in the affected countries and to strengthen systems in neighboring countries to detect importations and rapidly respond. There are also funds within the emergency funding request for the Global Health Security Agenda.
- The Office of the Assistant Secretary for Preparedness and Response's (ASPR) Hospital Preparedness Program provides support for U.S. hospitals

Communications
- In response to a question about health communications in West Africa, Dr. Bell said that community mobilization is an important contributor to the success in Liberia
- In regard to domestic health communications following the Ebola cases in Dallas, Dr. Bell said that it is important for CDC to show the public what the public health system does and how it benefits them

Research & Development
- Research is ongoing to develop rapid diagnostic tests, treatments, and vaccines
- Dr. Bell reported that two candidate vaccines are under consideration for advanced clinical testing: one has completed Phase I safety trials, and one will finish Phase I trials soon. NIH plans to conduct a randomized controlled vaccine trial in Liberia, and CDC is designing a "step-wedge" protocol for testing one of the candidate vaccines in Sierra Leone.
- CDC is also conducting validation studies of the BioFire Ebola assay

Aftermath/Lessons Learned
- Once the outbreak is over, it will be important to make an inventory of lessons learned. One lesson is that communications and multi-partner health promotion activities were critical to the response effort.
- Another lesson concerns our renewed awareness of the vulnerability of a nation's healthcare infrastructure and how quickly it can crumble. CDC activities in the three affected countries and surrounding countries include efforts to strengthen healthcare facilities by improving infection control and facilitating basic improvements (e.g., ensuring adequate medical supplies and running water).
- In response to a question about sustaining improvements once the outbreak is over, Dr. Bell said that CDC hopes to carry forward some fundamental public health activities in the three affected countries, including better infection control in hospitals and other components of the Global Health Security Agenda.

➢ **Final comments/ Focused discussion:** ***Issues arising from long-term outbreak response efforts***

Dr. Khabbaz noted that the current response effort in West Africa is unprecedented in scope and may continue for some time. To get to zero we must sustain the response, working with partners and contractors to mobilize resources. The response continues to require the work of many staff members, including those in senior leadership positions. As a result, many other activities have been delayed or put on hold.

BSC Comments and Discussion
- CDC has had an incessant flow of emergency response requests over the years, each of which has diverted attention from routine public health tasks. CDC has learned from these experiences about incident management, flexibility, and how to better utilize its staff. Nevertheless, the Ebola outbreak is much bigger and more challenging than what CDC has faced before, and day-to-day work in some areas has suffered.
- When MERS-CoV cases increased in 2013, the public health community tried to communicate to policy-makers the urgent need for pandemic (or outbreak) preparedness. Because of the Ebola outbreak, this concern is even greater today, in terms of both domestic and global preparedness.
- In thinking about management strategies to improve pandemic preparedness, it might be useful to divide activities into three "buckets": outbreak response in affected countries; building underlying

infrastructure in vulnerable countries; and preparedness at home. CDC cannot fill all three buckets, but it can work with other federal agencies and other partners to identify roles and responsibilities, at home and abroad.

- Preparedness must be broad, because disease issues that are not at the forefront may be there tomorrow. Dr. Berkelman recalled that CDC had only one plague expert on staff when a plague outbreak occurred in India in 1994.
- The CDC emerging infectious disease reports of the 1990s warned about the dangers of disease spread in densely populated urban areas with poor or fragile healthcare infrastructures. This happened in 2014 when Ebola spread to Monrovia, Freetown, and Conakry.

➢ **Upcoming BSC/OID meeting**

The BSC/OID will convene for a day and a half meeting at CDC on May 6-7, 2015.

APPENDIX

Meeting Participants

BSC Members

Ruth Berkelman
Jack Bennett
Kristy Bradley
Mike Brady
Harry Chen
Frank Cockerill
Carole Heilman
Tim Jones
Ruth Lynfield
Beth Marlowe
Laurene Mascola
Steve Ostroff
Andy Pavia
Scott Ratzan
Guillermo Ruiz-Palacios
Susan Sharp
Jill Taylor
Jon Temte
Judy Wasserheit
Bob Weinstein

Partners and Public Visitors

Chris Aldridge *(National Association of County and City Health Officials)*
Andres Camacho-Gonzalez *(Pediatric Infectious Diseases Society)*
Jeff Engel *(Council of State and Territorial Epidemiologists)*
Jane Getchell *(Association of Public Health Laboratories)*
Patrick Joseph *(National Foundation for Infectious Diseases)*
Lilly Kan *(National Association of County and City Health Officials)*
Michael Hultner *(Lockheed-Martin)*

CDC Staff

Ed Ades
Aufra Araujo
Beth Bell
Elise Beltrami
Darbi Boulay
Chris Braden
Brian Breedlove
Christye Brown
Roberta Carey
Evelyn Cater
Bob Cottingham
Renee Crawford
Leslie Dauphin
Kim Distel
Thomas Byron Douglas
Peter Drotman
Susan Gerber
Jon Gentsch
Priscilla Golden
Cynthia Goldsmith
Tom Gomez
Marta Gwinn
Rita Helfand
Tom Hennessy
Harold Jaffe
Valerie Johnson
Saleem Kamili
Ellen Kersh
Rima Khabbaz
Preeta Kutty
Gayle Langley
Alexandra Levitt
Duncan MacCannell
Allison Maiuri
Laurie Markowitz
Tonya Martin
Rob Massung
Alison Mawle
Susan McClure
Marian McDonald
Jonathan Mermin
Nancy Messonnier
Steve Monroe
Jeff Morelli
Dale Morse
Robin Moseley
Eduardo O'Neill
Ismael Ortega-Sanchez
Mark Pallansch
Claudia Pappas
Jean Patel

CDC Staff (cont.)

Dan Payne
Larry Pickering
Bob Pinner
Sarah Poser
Scott Sammons
Michael Shaw
Sharon Slocumb
Steve Solomon
Rob Tauxe
Suxiang Tong
Lea Trujillo
John Watson
Stephanie Weaver
Sarah Wiley
Michelle Wilson

I hereby certify that to the best of my knowledge, the foregoing minutes of the proceedings of the meeting of the Board of Scientific Counselors, Office of Infectious Diseases, on December 10, 2014, are accurate and complete.

_/S/_____ __3/11/15_____

Ruth Berkelman, M.D. Date
Chair, BSC, OID